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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,856	09/11/2003	Eszter Birck-Wilson	GTC-56	5220

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,856	BIRCK-WILSON ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *22-30 and 45-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21, 31-44, and 57-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/27/04; 4/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group I, claims 1-21, 31-44, and 57-62, and the species of ion exchange chromatography in the paper filed 14 August 2006 is acknowledged. Claims 22-30 and 45-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 57-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-21, 31-44, and 57-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Applicant teaches ion exchange columns for the separation of IgG4 half and whole antibodies after acidification in a glycine-HCl buffer. Applicant provides no guidance to samples containing any other mixtures of half and whole antibodies amenable to use in the instant method other than to those containing IgG4. Other immunoglobulin isotypes are not

known to predictably produce such mixtures (see e.g. Angal et al., Mol. Immunol. 30: 105, 1993). Thus, one would not readily envision any other starting samples for use absent further guidance and unpredictable experimentation. Applicant also provides no guidance for the predictable separation of half and whole antibodies with other than samples containing IgG4 half and whole antibodies after acidification in a glycine-HCl buffer and ion exchange chromatography (see pages 23-24). In this regard citrate buffer is shown to aggregate (see Figs. 2A-2C), rather than, as does glycine-HCl buffer (see Figs. 3A-3D), to dissociate, IgG4 half antibodies. The ability of hydrophobic interaction columns to capture and to selectively release half and whole antibodies is not in evidence and would seem unpredictable absent further unguided experimentation. Thus, one would have to experiment further with other buffers and separation means with no guidance or predictability of success to randomly determine other functional conditions for IgG4 half and whole antibody separation. Such unguided, random, unpredictable experimentation is undue. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one

skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21, 31-44, and 57-62 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, "the" pH or mobility lack antecedent basis.

In claim 6 and claims dependent thereupon, "the" buffer lacks antecedent basis.

In claim 9, "the" ionic strength lacks antecedent basis.

In claim 31 and claims dependent thereupon, "the" pH or buffer or ionic strength lack antecedent basis.

Claims 58 and 62 do not further limit the subject matter of the prior claim from which they depend because a HIC column does not further limit the prior claimed ion exchange column.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 10, 12-15, 20, and 21 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by King et al. (Biochem. J. 281: 317, 1992).

King et al. reduced the pH of mixtures containing IgG4 half (including preparations of Fab') and whole (including $F(ab')_2$) chimeric or myeloma antibodies and applied the mixtures to series of columns including ion exchange columns. The eluted material was further separated by sodium dodecyl sulfate polyacrylamide gel electrophoresis, including with a rod (i.e. columnar) gel.

Claims 1, 2, 5, 8, 11, 12, 15, and 20 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Paulus (US 5,292,668).

Paulus lowered the pH of a mixture of Fab' monomers and $F(ab')_2$ IgG1 antibodies and separated the populations on a chromatography column (see e.g. cols. 8-9).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Angal et al. (Mol. Immunol. 30: 105, 1993) teach the chimeric antibody of King et al. having a further mutation in the hinge region to a sequence similar to that found in IgG1 and IgG2 which essentially abolishes the half IgG4 antibody molecules in the preparations. The reference suggests partial resolution of the half and whole antibodies by ion exchange chromatography, but does not provide details therefor (see page 105).

Schuurman et al. (Mol. Immunol. 38: 1, 2001) also provide IgG4 hinge mutants with reduced ability to form half antibody molecules.

Kretzschmar et al. (J. Immunol. Meth. 195: 93, 1996) teach lowering pH of a mixture of monomer and dimer single-chain Fv antibody molecules and column chromatography to separate them. However, the dimers are not covalently bound monomers.

Mezes et al. (US 6,329,507) teach lowering pH of a mixture of monomer and dimer single-chain Fv antibody molecules and column chromatography to separate them (see e.g. col. 24). However, the dimers are not covalently bound monomers.

Kutzko et al. (US 6,268,487) teach purification of proteins from milk, including antibodies made by transgenic animals.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James L. Grun, Ph.D.
October 26, 2006

LONG V. LE 10/27/06
SUPERVISORY PATENT EXAMINER
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